

IN THE CLAIMS:

1. – 85. (Cancelled)

86. (Previously Presented) A method of determining the presence of anti-Factor VIII allo-antibodies capable of degrading Factor VIII in a mammal, which comprises:

- i) isolating the plasma from a sample of blood taken from said mammal,
- ii) isolating anti-Factor VIII allo-antibodies from said plasma;
- iii) placing said anti-Factor VIII allo-antibodies in contact with Factor VIII for a period of time sufficient to permit any degradation of said Factor VIII by said anti-Factor VIII allo-antibodies; and
- iv) determining, after said period of time, whether said Factor VIII has been degraded by said anti-Factor VIII allo-antibodies.

87. (Previously Presented) The method of claim 86, wherein in step ii), said anti-Factor VIII allo-antibodies are isolated from said plasma by combining them with said Factor VIII.

88. (Previously Presented) The method of claim 87, wherein said Factor VIII is coupled to a matrix.

89. (Previously Presented) The method of claim 86, wherein in step ii), said anti-Factor VIII allo-antibodies are isolated by affinity chromatography.

90. (Previously Presented) The method of claim 89, wherein in step ii), said affinity chromatography comprises the use of Factor VIII covalently coupled to a Sepharose matrix.

91. (Previously Presented) The method of claim 90, wherein said Sepharose matrix is activated with cyanogens bromide.

92. (Previously Presented) The method of claim 86, wherein in step iii), said Factor VIII is labeled with a labeling agent.
93. (Previously Presented) The method of claim 92, wherein said labeling agent is a radio-labelling agent.
94. (Previously Presented) The method of claim 93, wherein said radio-labelling agent is ¹²⁵I.
95. (Previously Presented) The method of claim 86, wherein in step iii), said Factor VIII is placed in contact with the anti-Factor VIII allo-antibodies for a period of time of between about 0.5 and about 30 hours, at a temperature of about 15 to about 40°C.
96. (Previously Presented) The method of claim 86, wherein in step iii), said Factor VIII is placed in contact with the anti-Factor VIII allo-antibodies for a period of time of about 10 hours, at a temperature of about 15 to about 40°C.
97. (Previously Presented) The method of claim 86, wherein in step iii), said Factor VIII is placed in contact with the anti-Factor VIII allo-antibodies for a period of time of between about 0.5 and about 30 hours, at a temperature of 38°C.
98. (Previously Presented) The method of claim 86, wherein in step iii), said Factor VIII is placed in contact with the anti-Factor VIII allo-antibodies for a period of time of about 10 hours, at a temperature of 38°C.
99. (Previously Presented) The method of claim 86, wherein step iv) is carried out by a determination comprising a separation technique and a visualization technique.
100. (Previously Presented) The method of claim 99, wherein said separation technique is selected from the group consisting of gel electrophoresis, and gel filtration.

101. (Previously Presented) The method of claim 100, wherein said gel electrophoresis is SDS PAGE.
102. (Previously Presented) The method of claim 100, wherein said gel filtration is fast protein liquid chromatography gel filtration.
103. (Previously Presented) The method of claim 100, wherein said visualization technique is autoradiography.
104. (Previously Presented) The method of claim 86, which further comprises:
v) characterizing the site(s) in said Factor VIII molecule cleaved by said anti-Factor VIII allo-antibodies.
105. (Previously Presented) The method of claim 104, wherein said characterization is carried out by placing said Factor VIII in contact with said anti-Factor VIII allo-antibodies capable of degrading Factor VIII, separating and then sequencing the fragments of Factor VIII resulting therefrom.
106. (Previously Presented) The method of claim 105, wherein said separation is carried out using a gel electrophoresis technique.
107. (Previously Presented) The method of claim 106, wherein said separation is SDS PAGE.
108. (Previously Presented) The method of claim 105, wherein said sequencing is carried out using an N-terminal sequencing technique.
109. (Previously Presented) The method of claim 108, wherein said sequencing carried out using an N-terminal sequencing technique is by using an automatic protein microsequencer.

110. (Previously Presented) The method of claim 105, wherein said sequencing locates scissile bonds between the A1 and A2 domains, on the N-terminus of the A3 domain and within the A3 domain of the Factor VIII molecule.

111. – 154. (Cancelled)